Injury, Int. J. Care Injured 50 (2019) 2097–2102

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Hyperglycemia as a risk factor for postoperative early wound infection after bicondylar tibial plateau fractures: Determining a predictive model based on four methods

Andres Rodriguez-Buitrago[a,e], Attum Basem[a], Ebubechi Okwumabua[b], Nichelle Enata[b], Adam Evans[b], Jacquelyn Pennings[c], Bernes Karacay[c], Mark John Rice[d], William Obremskey[a,*]

[a] Division of Orthopaedic Trauma, Vanderbilt Medical Center, 1215st Avenue South, Nashville, TN, 37212, United States
[b] Meharry Medical College, 1005 Dr DB Todd Jr Blvd, Nashville, TN, 37208, United States
[c] Department of Orthopaedics, Vanderbilt Medical Center, 1215 21st Avenue South, Nashville, TN, 37212, United States
[d] Department of Anesthesiology, Vanderbilt Medical Center, 1215 21st Avenue South, Nashville, TN, 37212, United States
[e] Universidad del Rosario, School of Medicine and Health Sciences, Bogotá, Colombia

ARTICLE INFO

Keywords:
Orthopaedic trauma
Tibial plateau fractures
Infection
Surgical site infection
Hyperglycemia

ABSTRACT

Objectives: Identify a glucose threshold that would put patients with isolated bicondylar tibial plateau fractures at risk of early wound infection (i.e. < 90 days).
Design: Retrospective review of medical records.
Setting: Academic American College of Surgeons (ACS) Level 1 trauma center.
Patients: Adult patients between 2010 and 2015 with an operatively treated isolated bicondylar tibial plateau fracture and at least three glucose measurements during their hospitalization.
Main Outcome Measurement: To predict infection using four different methods: maximum preoperative blood glucose (PBG), maximum blood glucose (MGB), Hyperglycemic Index (HGI), and Time-Weighted Average Glucose (TWAG).
Results: 126/381 patients met our inclusion criteria. Fifteen (12%) patients had an open fracture and 30/126 (23%) developed an infection. Median glucose for each predictive method studied was 114 (IQR 101.2–137.8) mg/dL for PBG, 144 (IQR 119–169.8) mg/dL for MBG, 0.8 (IQR 0.20–1.60) mmol/L for HGI, and 120.4 (IQR 106.0–135.6) mg/dL for TWAG. As expected, infected patients had higher PBG, MGB, and TWAG. HGI was similar in both groups. None of these differences prove to be statistically significant ($p > .05$). Logistic regression models for all the methods showed that having an open fracture was the strongest predictor of infection.
Conclusion: It is well known that stress-induced hyperglycemia increases the risk of infection, we present and compare four models that have been used in other medical fields. In our study, none of the methods presented identified a glucose threshold that would increase the risk of infection in patients with bicondylar tibial plateau fractures.
Level of Evidence: Retrospective review, Level III. See Instructions for Authors for a complete description of levels of evidence.

Introduction

Tibial plateau fractures are common injuries of the lower extremity with reported wound complications rates as high as 88% and infection rates that range from 5% to 15% [1–4]. Known risk factors for developing an infection are: smoking status, diagnosis of diabetes, open fracture, presence of compartment syndrome, prolonged operative times, and high energy fractures (i.e. Schatzker IV-VI) [3,5–7]. Hyperglycemia is common after high-stress events. Stress-induced hyperglycemia has been widely

* Corresponding author.
E-mail addresses: andres.rodriguez@vumc.org (A. Rodriguez-Buitrago), basem.a.attum@vumc.org (A. Basem), neokwumabua17@email.mmc.edu (E. Okwumabua), nharrison17@email.mmc.edu (N. Enata), aevans17@email.mmc.edu (A. Evans), jacquelyn.pennings@vanderbilt.edu (J. Pennings), bernes.karacay.1@vumc.org (B. Karacay), mark.j.rice@vanderbilt.edu (M.J. Rice), william.obremskey@Vanderbilt.edu (W. Obremskey).

https://doi.org/10.1016/j.injury.2019.07.028
0020-1383/

studied in other medical fields (e.g. intensive care populations and surgical patients) and has been shown to correlate with higher risk of infection in orthopedic and trauma patients as well as with mortality in patients in the intensive care unit. Hyperglycemia is thought to predispose patients to infection by altering the normal immune response and endothelium, increasing the susceptibility to oxidative stress, and increasing inflammation [8–13]. Several studies in other different medical fields have been able to identify a glycemic threshold that increases the risk of postoperative infection and have highlighted the importance of perioperative glucose control [14–17].

Using four different methods that have already been published, we aimed to identify a predictive glucose value that would serve as a prognostic marker for early wound infection in patients with isolated bicondylar tibial plateau fractures. To our knowledge, this is the first study in the orthopaedic literature comparing these four different methods.

Methods

Following Institutional Review Board approval, we identified patients over 18-years-old at the time of injury with an isolated bicondylar tibial plateau fracture that was operatively-treated (CPT code 37536) between 2010 through 2015. Patients were excluded if they had any documented active infection at the time of admission or if they had less than three glucose values during their index hospitalization. Medical records were reviewed to collect demographic (sex, smoking status, diagnosis of diabetes), hospitalization (glucose values during the definitive fixation hospitalization), and injury (type of fracture, Injury Severity Score [ISS], staged procedure, and diagnosis of infection) related variables. No information regarding the type of diabetes and treatment was collected. Since HgA1C is not required for any of the calculations and is not consistently obtained, this variable was not collected.

Definition of surgical site infection

Medical records were reviewed to identify patients that had a documented diagnosis SSI within 90 days of their study injury, required a reoperation for infection and had a positive intraoperative culture, pathology specimens, or visible gross purulence at the operative site. Superficial infections treated with only with oral or topical antibiotics were not included in the study.

All injuries were treated by a Trauma fellowship trained orthopaedic surgeon at a Level I Trauma Hospital. Open fractures were treated in a standard manner. Antibiotics were given as soon as possible in the emergency department, with type 1 and type 2 fractures (according to the Gustilo-Anderson [GA] classification) receiving cefazolin (Ancef) and type 3 fractures receiving cefazolin and a fluoroquinolone. This was followed by irrigation and debridement; depending on the soft tissue status and fracture pattern decision between single or stage fixation was made. In those cases where an external fixation was used, open reduction and internal fixation was performed 2–3 weeks later. Vascular surgery and Plastics were consulted when appropriate to manage vascular and soft tissue injuries, respectively. Compartment syndrome was clinically diagnosed by a trauma fellowship trained orthopaedic surgeon.

For each patient, the Maximum Preoperative Glucose (PBG) and Maximum Blood Glucose level (MBG) during the whole hospitalization were identified and collected. Glucose values and length of stay were collected to calculate the Hyperglycemic Index (HGI) and the Time-Weighted Average Glucose (TWAG). The HGI provides one value that is representative of glucose measures and length of stay and is defined as the area under the curve above of all glucose values divided by the length of stay. By doing this, an index value that is independent of the length of stay will be the result. Based on prior studies, an HGI greater than 1.72 mmol/L is categorized as hyperglycemia [9,18–21].

The TWAG provides one unique glucose value for every patient studied, it is a representation of all the measured blood glucose values and the time intervals at which they were measured [12,13,16]. As suggested by Yoo et al, it is reasonable to use this method since patients have different progression, variable length of stay, glucose values, and intervals in which they were taken [16]. The use of TWAG aims to minimize bias caused by blood glucose intervals.

It can be calculated with the following equation:

$$TWAG = \frac{[(X_1 + X_2)(T_1 - T_2) + (X_2 + X_3)(T_3 - T_2) + (X_{n-1} + X_n)(T_n - T_{n-1})]}{2\ x\ (T_n - T_{n-1})}$$

Where T represents the time of measurement, and X the blood glucose level.

Descriptive statistics were performed for demographic data. Glucose values collected were strongly skewed to the right, necessitating the reporting of median and interquartile range (IQR). Differences between measures were tested by infection status using a Mann-Whitney test due to skewed distributions of glucose measures. Logistic regressions for the different independent variables (ISS, fracture type [open vs. closed], smoking status, PBG, MBG, HGI, and TWAG) were conducted to predict infection. No more than two predictors were tested together due to the small number of patients who developed infection. **F**inally, a Receiver Operator Characteristic (ROC) curve was plotted to compare the different methods analyzed to predict infection. For analysis, $p < .05$ was considered to be statistically significant. Analysis was performed using SPSS® (IBM Corp. Released in 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.)

Results

Three hundred and eighty-one patients were initially identified based on CPT codes, 126 (33%) patients met our inclusion criteria. Sixty-nine (54%) were males, with a mean age at the time of injury of 52 ± 15 (range, 21 to 89) years and 15 (41%) were smokers at the time of their injury. Seventeen (13%) patients had a prior diagnosis of diabetes. No differentiation was made between type 1 or type 2 diabetes mellitus, time from diagnosis, or treatment. Fifteen (12%) patients had an open fracture, 7 of them (47%) developed an infection. Compartment syndrome was identified in 19 (15%) patient. Fractures were treated in a staged fashion in 84/126 (67%) cases. Diagnosis of infection was made in 30/126 (23%) patients, with a median time of diagnosis of 4.8 ± 3.5 weeks. Of these, 4/30 (19%) patients had a diagnosis of diabetes. (Table 1)

For all the patients combined, median PBG was 114 (IQR 101.2–137.8) mg/dL and MBG was 144 (IQR 119–169.8) mg/dL; median HGI was to be 0.8 (IQR 0.34–1.64) mmol/L while median TWAG was 120.4 (IQR 110–136.64) mg/dL. Table 2 presents the calculated and collected values based on infection status. Comparison did not reveal statistically significant differences between infected and non-infected patients for PBG (median: infected =120.5 mg/dL vs. non-infection =114 mg/dL; $p = 0.83$), MBG (median: infected 147 mg/dL vs. non-infection =143 mg/dL; $p = 0.68$), or TWAG (median: infection =120.6 mg/dL vs. non-infection =119.6 mg/dL; $p = 1.00$). Median HGI was similar in both groups (0.8 mmol/L; $p = 1.00$).

A multivariable logistic regression was made to determine whether the covariates of fracture type, smoking status, or ISS affected the relationship between blood glucose summary variables and the outcome of infection. A series of four models were run predicting infection from each of the method studied (PBG, MBG, HGI, and TWAG) and the other independent variables

Table 1
Patient demographics (N = 126).

Patient and fracture characteristics		
Sex		
Female	57	(46%)
Male	69	(54%)
Age		
Mean ± SD	52 ± 15	
Range	21 - 89	
Smoker		
Yes	52	(41%)
No	74	(59%)
Diabetic		
Yes	17	(13%)
No	109	(87%)
ISS		
Mean ± SD	11 ± 7	
Range	4 - 38	
Fracture type		
Open	15	(12%)
Closed	111	(88%)
Compartment syndrome		
Yes	19	(15%)
No	107	(85%)
Staged surgery		
Yes	83	(66%)
No	43	(34%)
Infection		
Yes	30	(23%)
No	96	(77%)
Time to infection (weeks)		
Mean ± SD	4.8 ± 3.5	
Range	0.4 - 11	

Table 2
Median glucose values for each of the methods studied.

Comparison of the different methods evaluated				
	Median	IQR	Min.	Max.
All patients (N = 126)				
PBG	114.0	(101.2–137.8)	59.0	477.0
MBG	144.0	(119.0–169.8)	85.0	639.0
TWAG	120.4	(106.0–135.6)	0.0	237.8
HGI	0.8	(0.20–1.60)	0.0	7.2
Not infected (N = 96)				
PBG	114.0	(99.2–137.2)	59.0	477.0
MBG	143.0	(116.5–170.0)	85.0	639.0
TWAG	119.6	(105.8–135.7)	0.0	237.8
HGI	0.8	(0.34–1.64)	0.0	7.2
Infected (N = 30)				
PBG	120.5	(105.5–138.5)	81.0	230.0
MBG	147.0	(162.2–165.0)	86.0	331.0
TWAG	120.6	(110.0–133.4)	94.5	200.4
HGI	0.8	(0.3–1.50)	0.0	5.1

IQR: Interquartile Range.
PBG: maximum preoperative blood glucose value, **MBG:** maximum blood glucose value during the index hospitalization; **HGI:** Hyperglycemic Index; **TWAG:** Time-Weighted Average Glucose.

(ISS, smoking status and type of fracture). These models confirm the bivariate analysis results, showing that neither PBG, MBG, HGI, or TWAG significantly predict infection, even when controlling for other risk factors ($p > 0.05$). These models consistently show that fracture type is a significant predictor of infection, with patients with an open fracture having higher odds of infection when compared to those with a closed fracture (OR = 3.28 to 3.39, $p < .05$). Smoking status and ISS did not significantly predict infection when controlling for fracture type and the predictive methods. (Table 3) (Fig. 1)

Fig. 2 further confirm the results, showing that in all the ROC curves of PBG, MBG, TWAG and HGI, the areas under the curve were low (0.54, 0.51, 0.52, and 0.50 respectively). None of them prove to be statistically significant. Since the effect sizes were very low, a power analysis revealed that increasing the sample size would not be likely to produce significant results (to detect statistically significant differences in both groups (infected vs. non-infected) we would need at least 12,888 patients for the HGI model and at least 43,562 in the TWAG model).

Due to the significant effects of fracture type (open vs closed) in the logistic regression models, a subgroup analysis excluding patients with an open fracture was conducted (N = 111) using bivariate Mann-Whitney tests to check for median differences in each predictive method (PBG, MBG, HGI, and TWAG) by infection status (N = 23 [20.7%] infected patients). Median values were similar to the full sample across all four methods; PBG = 114 (IQR 101.5–137.5) mg/dL, MBG = 144 (IQR 115–169.5) mg/dL, HGI = 0.8 (IQR 0.2–1.6) mmol/L for HGI, and TWAG = 120.9 (IQR 106–135.7) mg/dL. Similarly, when comparing the collected values for each predictive method based on infection status, infected patients did not have significantly different PBG (median: infected =130 mg/dL vs. non-infection =113.5 mg/dL; $p = 0.36$), MBG (median: infected 147 mg/dL vs. non-infection =143 mg/dL; $p = 0.25$), HGI (0.8 mmol/L, $p = 1.00$), or TWAG values (median: infection =120.9 mg/dL vs. non-infection =121.1 mg/dL; $p = 1.00$). A post-hoc power analysis using the effect sizes from the current data concluded that, although differences were slightly larger in the closed fracture subgroup, the effect sizes are still very small and 1230 patients with a closed bicondylar tibial plateau would be needed to achieve significance with the HGI method while 1826 patients would be required for the TWAG method.

Discussion

This study sought to identify a unique glucose value that would increase the risk of early wound infection in patients with an operatively treated bicondylar tibial plateau fracture using four different methods to evaluate glucose (i.e. maximum perioperative hyperglycemia [MPG], maximum blood glucose [MBG] during the hospitalization, hyperglycemic index [HGI], and time-weighted average glucose [TWAG]). Tibial plateau fractures are known to have a high risk of infection and this is a major concern when treating this injury as patients are who develop infection often must be placed on long-term antibiotics, require additional surgeries, and require longer healing times. We believe that our inclusion criteria can explain why the infection rate presented in this study (23%) is higher than what its commonly reported in the literature [3], as patients with worse injuries, prolonged hospital stay, and staged fixations were more likely to have more blood tests done and, therefore, more glucose values.

In this study, a previous diagnosis of diabetes was not a good indicator of postoperative infection nor was MBG. Prior studies have shown that in elective arthroplasty surgery infected patients had a significantly higher preoperative, perioperative, and postoperative blood glucose when compared to those who did not develop an infection; in nondiabetic patients, a morning blood glucose greater than 140 mg/dL on postoperative day 1 had a threefold increase in risk for infection compared to non-infected patients [22]. On the other hand, Mraovic et al identified diabetes mellitus and morning postoperative glucose as predictors of postoperative infection after total joint arthroplasty [22]. Richards et al studied almost 800 patients with orthopedic injuries indicating that more than one glucose value greater than 200 had a 4.4% infection rate compared to 1.6% in patients without more than one glucose level of greater than 200 [19].

Table 3
Logistic regression model for each of the methods studied.

	PBG method			MBG method			HGI method			TWAG method		
	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Open Fracture	3.39	1.05 – 10.93	**0.038**	3.33	1.03 - 10.70	**0.041**	3.34	1.04 – 10.7	**0.040**	3.34	1.04 - 10.76	**0.040**
Smoker	1.01	0.95 - 1.08	0.861	1.00	0.95 - 1.07	0.923	1.00	0.95 – 1.07	0.920	1.00	0.95 - 1.07	0.915
ISS	1.59	0.68 – 3.76	0.283	1.53	0.65 - 3.61	0.324	1.53	0.65 - 3.62	0.327	1.54	0.64 - 3.68	0.332
PBG	1.00	0.99 - 1.01	0.568									
MBG				1.00	1.00 – 1.01	0.758						
HGI							1.04	0.77 – 1.50	0.795			
TWAG										1.00	0.99 – 1.01	0.895

OR: Odds Ratio; **CI**: Confidence Interval.
ISS: Injury Severity Score; **PBG**: maximum preoperative blood glucose value, **MBG**: maximum blood glucose value during the index hospitalization; **HGI**: Hyperglycemic Index; **TWAG:** Time-Weighted Average Glucose.

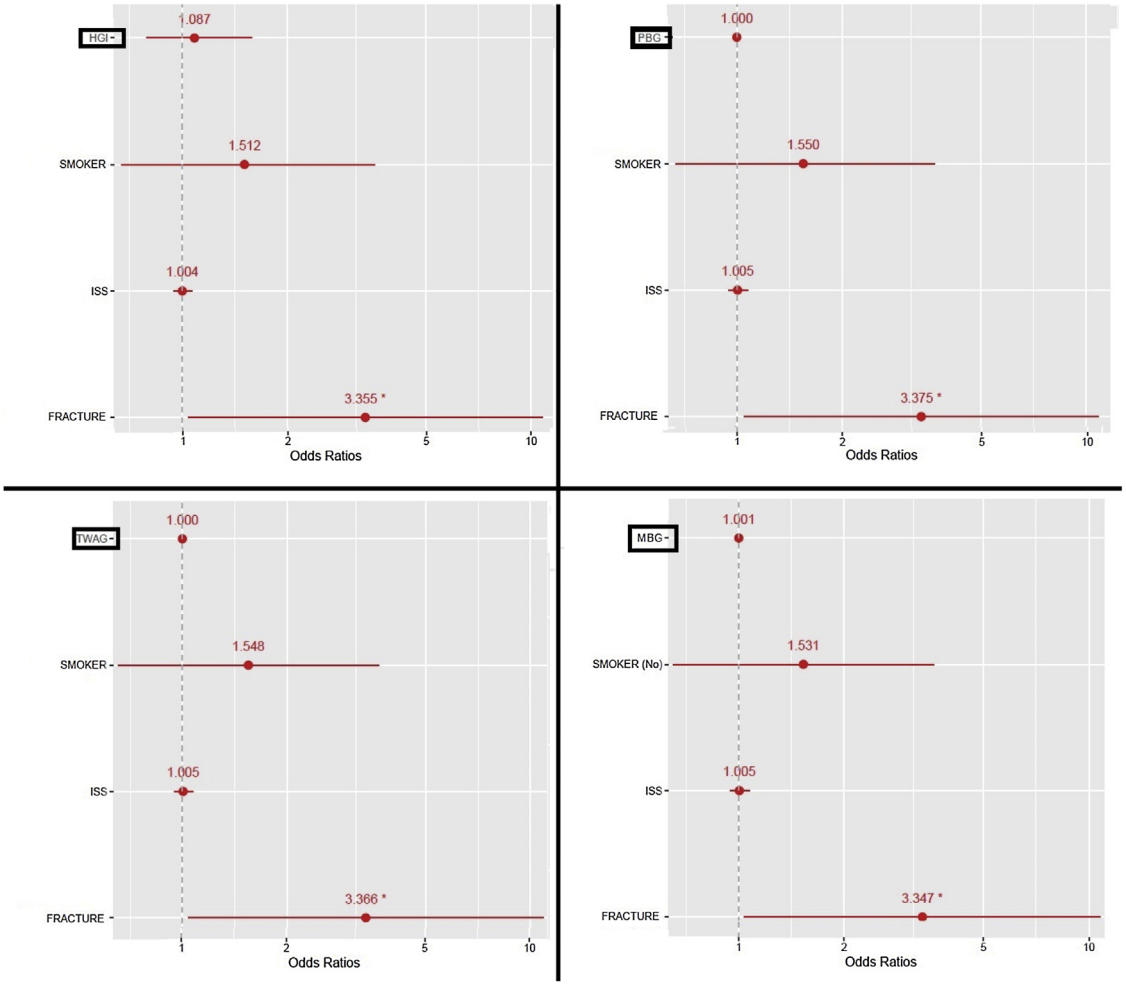

Fig. 1. Odds Ratio for each predictive method evaluated.
Odds ratio of the four predictive methods studied. With every method, the only determinant of infection was having an open fracture.

Although HGI had a slightly higher odds ratio when compared to the other methods presented, it did not prove to be statistically significant; median HGI was 0.8 mmol/L, (OR of 1.04; 95% IC 0.77–1.5; p = .8) for infected and non-infected patients. Prior studies have shown that, when compared to other glucose measurements, HGI is a good predictor of postoperative complications in patients treated in the intensive care unit, and patients with a higher HGI ($\geq$ 1.76) have a higher risk of infection when to those with a lower HGI (7.5% vs. 1.7%) [9,19,21]. In a study including non-diabetic orthopaedic trauma patients treated in the trauma unit an HGI as close to zero before, during, and after surgery, showed to improve the surgical outcome versus an HGI of greater than 8 mmol/L [9]. This discrepancy, **compared** with other orthopaedic literature could be explained due to our decision to only include patients with an isolated bicondylar plateau; Richards et al. [9] evaluated HGI on non-diabetic patients admitted to the ICU. In our study, prior diagnosis of diabetes did not show to correlate with infection.

Studies have shown that the greatest indicator of postoperative complications was elevated glucose levels during the perioperative period compared to diabetes status. Chulsoo et al reported that intraoperative glucose levels greater than 200 mg/dL were an

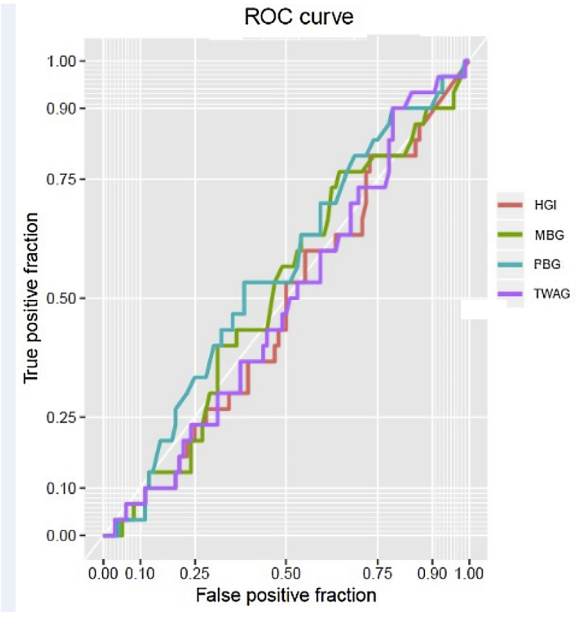

Fig. 2. Receiver operator characteristic (ROC) curves comparing the different predictive methods evaluated.
Areas under the curve are 0.54 for Preoperative Blood Glucose (PBG), 0.51 for Maximum Blood Glucose (MBG), 0.50 for Hyperglycemic Index (HGI) and 0.52 for Time-weighted average glucose (TWAG).

independent risk factor for surgical site infection after liver transplant [14]. Rogers et al found that postoperative hyperglycemia increased the risk of postoperative infection by 30% with every 40-point increase from normoglycemia (<110 mg/dL), their study concluded that increased risk of postoperative infection caused by postoperative hyperglycemia is independent of diabetes status [15]. Kwon's study with over 11,000 patients who had glucose levels monitored postoperatively during days 0, 1, and 2 had a 29.1% rate of hyperglycemia [23]. After clinical factors were controlled, hyperglycemic patients had a significantly increased risk of infection (OR 2.0; 95% CI, 1.63–2.44), preoperative interventions (OR, 1.8; 95% CI, 1.41–2.3), and death (OR, 2.71; 95% CI, 1.72–4.28). A dose-effect relationship was identified between insulin related to glucose control and (worst 180–250 mg/dL, best <130 mg/dL) outcome. As it has been shown in prior studies, the results of this study showed that having an open fracture was the strongest predictor of infection (OR ranging from 3.28 to 3.39) and was the only statistically significant variable.

Our study had several limitations. Even though we evaluated objective data in our study, it has the inherent biases of any retrospective study. Our sample size was limited due to our inclusion criteria (isolated fractures with more than three glucose values), this could have introduced some level of selection bias as patients with worse injury patterns, staged fixation, or prolonged hospital stay were more likely to be included in our study. We don't believe that this bias affected our results. We limited our study to identify the risk of early wound infection (<90 days), two patients developed an infection after this time period. The inclusion of those patients will not alter our results. As shown with the post-hoc analysis, to show significance with the methods evaluated we would need an approximate sample size of at least 12,888 patients for the HGI model and at least 43,562 in the TWAG. We believe that this study adds to the literature as it analyzes and compares different predictors of infection that are not usually considered in the orthopaedic literature. It is our hope that this study paves the way for a larger retrospective or prospective study aiming to identify a glucose threshold that will put orthopaedic patients at risk for developing infection.

Conclusion

Stress-induced hyperglycemia has shown to increase the risk of infection and we have presented and compared four models that have been used in other specialties. In our study, having an open fracture was a strong predictor for the development of early surgical site infection. None of the four methods presented identified a glucose threshold that would increase the risk of infection in patients with bicondylar tibial plateau fractures.

References

[1] Berkson EM, Virkus WW. High-energy tibial plateau fractures. J Am Acad Orthop Surg 2006;14(1):20–31.
[2] Young MJ, Barrack RL. Complications of internal fixation of tibial plateau fractures. Orthop Rev 1994;23(2):149–54. http://www.ncbi.nlm.nih.gov/pubmed/8196973.
[3] Morris BJ, Unger RZ, Archer KR, Mathis SL, Perdue a M, Obremskey WT. Risk factors of infection after ORIF of bicondylar tibial plateau fractures. J Orthop Trauma 2013;27(9):196–200, doi:http://dx.doi.org/10.1097/BOT.0b013e318284704e.
[4] Barei DP, Nork SE, Mills WJ, Henley MB, Benirschke SK. Complications associated with internal fixation of high-energy bicondylar tibial plateau fractures utilizing a two-incision technique. J Orthop Trauma 2004;18(10):649–57, doi:http://dx.doi.org/10.1097/00005131-200411000-00001.
[5] Momaya AM, Hlavacek J, Etier B, et al. Risk factors for infection after operative fixation of Tibial plateau fractures. Injury 2016;47(7):1501–5, doi:http://dx.doi.org/10.1016/j.injury.2016.04.011.
[6] Colman M, Wright A, Gruen G, Siska P, Pape HC, Tarkin I. Prolonged operative time increases infection rate in tibial plateau fractures. Injury 2013;44(2):249–52, doi:http://dx.doi.org/10.1016/j.injury.2012.10.032.
[7] Castillo RC, Bosse MJ, MacKenzie EJ, Patterson BM, LEAP Study Group. Impact of smoking on fracture healing and risk of complications in limb-threatening open tibia fractures. J Orthop Trauma 2005;19(3):151–7, doi:http://dx.doi.org/10.1097/00005131-200503000-00001.
[8] Kerby JD, Griffin RL, MacLennan P, Rue LW. Stress-induced hyperglycemia, not diabetic hyperglycemia, is associated with higher mortality in trauma. Ann Surg 2012;256:446–52, doi:http://dx.doi.org/10.1097/SLA.0b013e3182654549.
[9] Richards JE, Kauffmann RM, Obremskey WT, May AK. Stress-induced hyperglycemia as a risk factor for surgical-site infection in non-diabetic orthopaedic trauma patients admitted to the intensive care unit. J Orthop Trauma 2012;1:, doi:http://dx.doi.org/10.1097/BOT.0b013e31825d60e5.
[10] Butler SO, Btaiche IF, Alaniz C. Relationship between hyperglycemia and infection in critically ill patients. Pharmacotherapy 2005;25(7):963–76, doi:http://dx.doi.org/10.1592/phco.2005.25.7.963.
[11] Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: a review of pathogenesis. Indian J Endocrinol Metab 2012;16:S27–36, doi:http://dx.doi.org/10.4103/2230-8210.94253.
[12] Badawi O, Yeung SY, Rosenfeld BA. Evaluation of glycemic control metrics for intensive care unit populations. Am J Med Qual 2009;24(4):310–20, doi:http://dx.doi.org/10.1177/1062860609336366.
[13] Badawi O, Waite MD, Fuhrman SA, Zuckerman IH. Association between intensive care unit-acquired dysglycemia and in-hospital mortality. Crit Care Med 2012;40(12):3180–8, doi:http://dx.doi.org/10.1097/CCM.0b013e3182656ae5.
[14] Park C, Hsu C, Neelakanta G, et al. Severe intraoperative hyperglycemia is independently associated with surgical site infection after liver transplantation. Transplantation 2009;87(7):1031–6, doi:http://dx.doi.org/10.1097/TP.0b013e31819cc3e6.
[15] Rogers SO, Ramos M, Khalpey Z, et al. Relationship of perioperative hyperglycemia and postoperative infections in patients who undergo general and vascular surgery. Ann Surg 2008;248(4):585–90, doi:http://dx.doi.org/10.1097/SLA.0b013e31818990d1.
[16] Yoo S, Lee H-J, Lee H, Ryu H-G. Association between perioperative hyperglycemia or glucose variability and postoperative acute kidney injury after liver transplantation: a retrospective observational study. Anesth Analg 2017;124(1):35–41, doi:http://dx.doi.org/10.1213/ANE.0000000000001632.
[17] Scalea TM, Bochicchio GV, Bochicchio KM, Johnson SB, Joshi M, Pyle A. Tight glycemic control in critically injured trauma patients. Ann Surg 2007;246(4):605–10, doi:http://dx.doi.org/10.1097/SLA.0b013e318155a789.
[18] Vogelzang M, van der Horst ICC, Nijsten MWN. Hyperglycaemic index as a tool to assess glucose control. Crit Care 2004;8(3):R122–7, doi:http://dx.doi.org/10.1186/cc2840.
[19] Richards JE, Kauffmann RM, Zuckerman SL, Obremskey WT, May AK. Relationship of hyperglycemia and surgical-site infection in orthopaedic surgery. J Bone Jt Surg - Ser A 2012;94(13):1181–6, doi:http://dx.doi.org/10.2106/JBJS.K.00193.

[20] Vogelzang M, Nijboer JMM, Van Der Horst ICC, Zijlstra F, Ten Duis HJ, Nijsten MWN. Hyperglycemia has a stronger relation with outcome in trauma patients than in other critically ill patients. J Trauma - Inj Infect Crit Care 2006;60 (4):873–7, doi:http://dx.doi.org/10.1097/01.ta.0000195715.63978.80.
[21] Vogelzang M, van der Horst ICC, Nijsten MWN, et al. Hyperglycaemic index as a tool to assess glucose control: a retrospective study. Crit Care 2004;8(3):R122–7, doi:http://dx.doi.org/10.1186/cc2840.
[22] Mraovic B, Suh D, Jacovides C, Parvizi J. Perioperative hyperglycemia and postoperative infection after lower limb arthroplasty. J Diabetes Sci Technol 2011;5(2):412–8, doi:http://dx.doi.org/10.1177/193229681100500231.
[23] Kwon S, Thompson R, Florence M, et al. Beta-blocker continuation after noncardiac surgery: a report from the surgical care and outcomes assessment program. Arch Surg 2012;147(5):467–73, doi:http://dx.doi.org/10.1001/archsurg.2011.1698.